REMARKS

Claims 36 to 44 were pending in the application before entry of the present amendment. Claims 40 and 41 have been canceled without prejudice. Applicants reserve their right to prosecute the subject matter of claims 40 and 41 in one or more related continuation, continuation-in-part or divisional applications. Claims 42 and 44 have been amended to more clearly point out what Applicants consider the invention. New claims 45 to 49 have been added to more clearly point out what Applicants consider as the invention. Support for the new claim can be found in the application as filed, *e.g.*, the chart below. Thus, no new matter has been introduced. Claims 36 to 39 and 42 to 49 are pending upon entry of the present amendment.

Claim	Support
42	Page 20, lines 29 to 31
44	Page 20, lines 29 to 31
45, 46	Page 88, line 1 to page 90, line 10; page 20, lines 29 to 31
47, 48	Page 90, line 14 to page 91, line 26; page 87, lines 9 to 11
49	Page 87, lines 19 to 22
50	Page 90, line 14 to page 91, line 26

THE REJECTIONS UNDER 35 U.S.C. § 112 SHOULD BE WITHDRAWN

Claims 40 and 41 were rejected under section 112, first paragraph, of Title 35 of the United States Code allegedly for lack of enabling support in the specification. The Examiner bases this rejection on the allegation that the specification does not provide evidence that every embodiment of the claimed invention has the claimed properties. Applicants contend that this rejection is in error. However, in view of the present cancellation of claims 40 and 41 this rejection is moot.

Claims 42 and 43 were rejected under 35 U.S.C. 112, first paragraph, for allegedly lacking enabling support. In particular, the Examiner contends that the scope of the claim is not enabled because Applicants have allegedly not demonstrated that the specifically claimed truncations are likely to result in operable inventions. Applicants respectfully contend that this rejection is in error and that the full scope of the claims is enabled.

Claim 42 has been amended to recite that the viral particle "exhibits a lower degree of virulence as compared to a wild type virus." Applicants submit that the description found in the specification as filed is adequate since it provides ample guidance for how to make and use the claimed respiratory syncytial virus that exhibits a lower degree of virulence as compared to a wild type virus. The specification as filed teaches that C-terminal deletions of the M2-1 protein can be introduced to generate an attenuated recombinant RSV, see, *e.g.*, the specification at page 15, line 20 and at page 87, lines 25 to 28. Examples for how such truncations can be introduced into the M2-1 protein are presented in section 12.2 (page 90, line 14 to page 91, line 26) of the specification as filed. *E.g.*, the specification at section 6 (page 27, line 23 to page 30, line 5) provides teachings of how the recombinant virus can be rescued. Throughout the specification as filed, teachings can be found that relate to the determination of whether a recombinant RSV is attenuated. As described in the specification, an attenuated RSV is a virus that exhibits a lower degree of virulence as compared to a wild-type virus (the specification at page 20, lines 29 to 31). The virulence of a virus can be tested in various ways, *e.g.*, comparison of plaque morphology (the specification at page 63, lines 13-21) and growth kinetics (the specification at page 63, line 22 to page 64, line 8).

Further, Applicants respectfully point out that procedures for testing whether a viral particle is attenuated are routine in the art, and that the skilled artisan would be able to determine without undue experimentation which of the viral particles are covered by the pending claims. Thus screening procedures to test the viral particles of the invention an attenuated phenotype should not be considered undue experimentation since such procedures are well-known and routine to the skilled artisan. Applicants would like to direct the Examiner's attention to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)):

> " 'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.' "

The Examiner admits that the determination of which truncations would and would not be operable would have been within the capacity of those skilled in the art. However, the Examiner continues that, because Applicants claim a series of <u>specific</u> truncations, the claims lack enabling support. First, Applicants respectfully point out that claim 42 is directed to any C-terminal truncation of the M2-1 protein that results in a virus with lower degree of

virulence. Descriptive support for such truncations can be found in the specification as filed, *e.g.*, at page 87, lines 25 to 28. Second, Applicants point out that the amount of experimentation that may be required to determine whether or not a particular C-terminal truncation results in a virus with an attenuated phenotype does not depend on where the truncation is introduced into the M2-1 protein. Thus, if the skilled artisan can determine without undue experimentation whether any C-terminal truncation is operable, the skilled artisan will also be capable to determine without undue experimentation whether a specific C-terminal truncation is operable.

Claim 44 has been rejected under 35 U.S.C. 112, first paragraph, for allegedly lacking enabling support in the specification. The Examiner argues that the scope of claim 44 is not enabled because the specification allegedly fails to provide sufficient guidance to determine which mutations in the M2-1 gene would result in the desired phenotype without undue experimentation. In particular, the Examiner argues that the claim reads on embodiments wherein the Histidine at position 25 of the protein is also mutated which would result in an inoperable species.

Claim 44 has been amended to recite that the viral particle "exhibits a lower degree of virulence as compared to a wild type virus." As set forth above in connection with the rejection of claims 42 and 43, Applicants submit that the description found in the specification as filed is adequate since it provides ample guidance for how to make and use the claimed respiratory syncytial virus that exhibits a lower degree of virulence as compared to a wild type virus. The specification as filed teaches at page 87, lines 9 to 11, that different point mutations and lesions can be combined in a single virus to generate an attenuated recombinant RSV. Examples for how such mutations can be introduced into the M2-1 protein are presented at page 21, line 1 to page 23, line 10 and in section 12 (page 87, line 1 to page 91, line 26) of the specification as filed. An exemplary teaching of how a recombinant virus can be rescued is provided in section 6 of the specification (page 27, line 23 to page 30, line 5). Throughout the specification as filed, teachings can be found that relate to the determination of whether a recombinant RSV is attenuated. As described in the specification, an attenuated RSV is a virus that exhibits a lower degree of virulence as compared to a wild-type virus (the specification at page 20, lines 29 to 31). The virulence of a virus can be tested in various ways, *e.g.*, comparison of plaque morphology (the specification at page 63, lines 13-21) and growth kinetics (the specification at page 63, line 22 to page 64, line 8). Thus, based on the guidance provided in the specification as filed and

on the information known in the art, the skilled artisan can determine without undue experimentation which mutations that are introduced in the virus in addition to the mutation at position 96 result in a viable virus.

Claim 44 is further rejected under 35 U.S.C. 112, first paragraph, for allegedly failing to comply with the written description requirement. In particular, claim 44 is rejected as allegedly containing new matter. Applicants respectfully disagree because the specification as originally filed provides written description of combinations of mutations and different mutations strategies.

The specification as filed teaches at page 87, lines 9 to 11, that different point mutations and lesions can be combined in a single virus to generate an attenuated recombinant RSV. Examples of mutations that can be introduced into the viral genome are presented at page 21, line 1 to page 23, line 10 and in section 12 (page 87, line 1 to page 91, line 26) of the specification as filed. Thus, the specification as filed provides written description for combinations of mutations, such as a combination of the mutations at position 96 of the M2-1 gene with other mutations in M2-1.

With regard to the Examiner's concern that claim 44 reads on amino acid substitutions at position 96 other than from cysteine to glycine, valine, aspartic acid and alanine, Applicants have amended the claim to recite that the amino acid is selected from the group consisting of to glycine, valine, aspartic acid and alanine.

Claim 44 is further rejected under 35 U.S.C. 112, second paragraph, because the claim recites that the cysteine at position 96 be substituted from "an amino acid selected from the group comprising glycine, valine, aspartic acid and alanine..." In accordance with the Examiner's suggestion, Applicants have amended the claim to recite that the amino acid is selected from the group consisting of to glycine, valine, aspartic acid and alanine. The Examiner further contends that the claim is indefinite because it is unclear how there can be more than one substitution for the same amino acid. In response, Applicants have deleted the recitation of "at least" in the claim.

Applicants assert that the instant specification in combination with information readily available to the skilled artisan at the time the instant application was filed fully enables the claimed invention and that the rejection under 35 U.S.C. § 112, first paragraph, should be withdrawn.

CONCLUSION

Applicants respectfully request that the amendments and remarks made herein be entered and made of record in the file history of the present application. Withdrawal of the Examiner's rejections and an allowance of the application are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

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